Qualitative and Quantitative Characterization of the *In Vitro* Dehydration Process of Hydrogel Contact Lenses

José M. González-Méijome,[1] Antonio López-Alemany,[2,3] José B. Almeida,[1] Manuel A. Parafita,[4] Miguel F. Refojo[5]

[1] Department of Physics (Optometry), School of Sciences, University of Minho, Braga, Portugal

[2] Ocular Surface, Cornea, and Contact Lens Research Group, Department of Optics, School of Optometry and Optics, University of Valencia, Spain

[3] Instituto de Oftalmología y Optometría de la Costera (IOOC), Novetlé, Spain

[4] Department of Surgery (Ophthalmology), School of Optics and Optometry, University of Santiago de Compostela, Spain

[5] Schepens Eye Research Institute, Harvard Medical School, Boston, Massachusetts

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Abstract: ***Purpose***: **To investigate the *in vitro* dehydration process of conventional hydrogel and silicone-hydrogel contact lens materials. *Methods*: Eight conventional hydrogel and five silicone-hydrogel contact lenses were dehydrated under controlled environmental conditions on an analytical balance. Data were taken at 1-min intervals and dehydration curves of cumulative dehydration (CD), valid dehydration (VD), and dehydration rate (DR) were obtained. Several quantitative descriptors of the dehydration process were obtained by further processing of the information. *Results*: Duration of phase I (r^2 = 0.921), CD at end of phase I (r^2 = 0.971), time to achieve a DR of −1%/min (r^2 = 0.946) were strongly correlated with equilibrium water content (EWC) of the materials. For each individual sample, the VD at different time intervals can be accurately determined using a 2nd order regression equation ($r^2 > 0.99$ for all samples). The first 5 min of the dehydration process show a relatively uniform average CD of about −1.5%/min. After that, there was a trend towards higher average CD for the following 15 min as the EWC of the material increases (r^2 = 0.701). As a consequence, average VD for the first 5 min displayed a negative correlation with EWC (r^2 = 0.835), and a trend towards uniformization among CL materials for the following periods (r^2 = 0.014). Overall, silicone-hydrogel materials display a lower dehydration, but this seems to be primarily due to their lower EWC. *Conclusions*: DR curves under the conditions of the present study can be described as a three-phase process. Phase I consists of a relatively uniform DR with a duration that ranges from 10 to almost 60 min and is strongly correlated with the EWC of the polymer as it is the CD during this phase. Overall, HEMA-based hydrogels dehydrate to a greater extent and faster than silicone-hydrogel materials. There are differences in water retention between lenses of similar water content and thickness that should be further investigated.** © 2007 Wiley Periodicals, Inc. J Biomed Mater Res Part B: Appl Biomater 83B: 512–526, 2007

Keywords: **gravimetry; hydration; hydrogel; silicone-hydrogel; contact lenses; dehydration**

INTRODUCTION

First, introduced by Wichterle and Lim[1] hydrogel materials have experienced a great expansion in healthcare industry, particularly for contact lens manufacture. However, despite the numerous improvements in their composition and manufacturing technology, the ocular performance of hydrogel contact lenses continues to be compromised by dehydration.

Dehydration begins immediately after a contact lens is placement on the eye and continues further during the day depending more or less on the material properties, lens thickness, environmental conditions and tear composition, and blink function.[2,3] End of the day complaints of dryness

Correspondence to: J. M. González-Méijome (e-mail: jgmeijome@fisica.uminho.pt)

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and other related symptoms, are at least in part attributed to dehydration of the lens on the eye.

In hydrogels, water uptake and release depend primarily on the chemical composition and crosslinking density of the polymer, thus determining the equilibrium water content (EWC) of the hydrogel. The thickness of the material also affects the degree of dehydration of contact lenses. But dehydration also affects other important properties of hydrogel contact lenses, such as oxygen permeability. In HEMA-based hydrogels oxygen permeability decreases as the lens dehydrates,[4] while in silicone-hydrogel lenses oxygen permeability increases as the polymer partially dehydrates.[5] Changes in lens parameters with dehydration have also been documented, as well as changes in lens movement on the eye.[6,7] Dehydration of hydrogel contact lenses has an impact on the ocular surface, since it is associated with surface deposit build-up, dryness symptoms, and dehydration of the corneal epithelium. Lens dehydration also has the potential to affect ionic and hydraulic permeability, thus reducing lens movement, promoting lens binding, and increasing the chance for microbial colonization due to limiting tear turnover and debris removal from the cornea–contact lens interface. Andrasko confirmed some of these effects as he observed that after lens insertion a new hydration equilibrium was reached, and the lenses became less flexible, less permeable to oxygen, and its base curve radius became steeper.[8]

Different approaches have been used to maximize water uptake and to minimize water release in hydrogel contact lens. Initially, the most common method was the introduction of other hydrophilic monomers into the base polymer, particularly into HEMA base hydrogels, such as, methacrylic acid, vinyl-pyrrolidone, and glyceryl methacrylate.[9] However, it was subsequently found that the higher the water uptake, the faster the water release while the lens is on the eye.[10] Biological deposit formation was also found to be a major factor in highly hydrated hydrogels contact lenses whether they are ionic or nonionic.[11,12] For this reason, modern materials include specific formulations claiming to prevent rapid dehydration from high water content materials, apparently with some clinical benefits.[13–16]

Despite the diversity of options, clinicians do not have objective indicators of the ability of different contact lenses to remain fully hydrated while they are on the eye and this limits their criteria to choose the right material for the right patient. This is more important in patients complaining of ocular contact lens discomfort related to dryness,[17,18] such as patients working in environments that could potentially exacerbate ocular symptoms,[19] older females, because of their higher risk to experience dryness with contact lenses,[20] and those with tear deficiency upon prefitting examination.[21]

Dehydration of contact lenses is usually measured by manual or automatic commercial refractometers.[22,23] However, the gravimetric method used in this study has been credited to be more precise for *in vitro* studies on the water content of hydrogel contact lenses.[24]

It has been reported that *in vitro* studies failed to explain the clinical observations that high water content lenses dehydrate more than low water content materials.[25] However, more recently, Jones et al. qualitatively characterized the dehydration process of hydrogel contact lenses under *in vitro* conditions.[26] Unfortunately, their work included fewer conventional hydrogel contact lenses, than the present study, and only the two silicon–hydrogel lenses available at the time the study was carried out. Also, they limited experiments to specific portions of the lenses, and the dehydration process was carried out under varying airflow conditions.

The present study was developed to investigate the dehydration process of eight HEMA-based hydrogel contact lenses, within more frequent EWC available, and the five silicone-hydrogel lenses also currently marketed. Different qualitative and quantitative indicators were developed to characterize the dehydration process of the samples and to compare against each other and to their respective EWC. The main goal was to obtain those parameters that more specifically characterize the *in vitro* dehydration process of conventional and silicone-hydrogel contact lens materials.

MATERIALS AND METHODS

Contact Lens Materials

Thirteen different commercial hydrogel contact lenses were used. Those materials were chosen to include the five silicone-hydrogel materials currently available and eight conventional HEMA-based hydrogel lenses; among these, including four hydrogel lenses claimed to maximize water uptake and minimize water release (omafilcon A, hioxifilcon A, B and pGMA+HEMA+MA copolymer). Their technical details are summarized in Table I. Three samples of each material from the same batch were measured.

Sample Preparation and Gravimetric Measurements

A digital analytical balance (AT 210, Metler Toledo, Giessen, Germany) with a six-figure scale capable of measuring within 0.001 mg was used to continuously measure the weigh of the contact lenses while they dehydrate at a controlled temperature of $(22.4 \pm 0.46)^{\circ}$C and a relative humidity (RH) of (49.1 ± 1.45)%. The accuracy of the instrument monitoring temperature and RH was $\pm 1^{\circ}$C and ± 5%, respectively. The weight of the lens was registered each 60 s with a microgram resolution ($\pm 1\ 10^{-6}$ grs).

Lenses were allowed to equilibrate for at least 24 h before testing in preservative-free saline solution meeting the criteria of BS EN ISO 10344:1998.[27] A number under each vial identified each lens and the investigator performing the measurements was not aware of the lens being measured.

After taking the lens from the vial, the excess water was removed by blotting with a slightly dampen Whatman No. 1 filter paper. The lens was then placed on a convex plastic

TABLE 1. Nominal Parameters of Contact Lenses Used in This Study

Brand	USAN Generic Name	Material (Main Monomers)	EWC (%)	Ionic (FDA)	Dk (barrer)	ST	CT (mm)
Air night & Day	Lotrafilcon A	TRIS+PDMS+NVP+DMA	24	No (I)	140	Plasma coating	0.080
Air Optix	Lotrafilcon B	TRIS+DMA+DMA	33	No (I)	110	Plasma coating	0.080
Purevision	Balafilcon A	TRIS+NVP+TPVC+NCVE+PBVC+	36	Yes (III)	99	Plasma oxidation	0.090
Acuvue Oasys	Senofilcon A	HEMA+PDMS+DMA+PVP	38	No (I)	103	No	0.070
Soflens 38	Polymacon	HEMA	38.6	No (I)	8.5	No	0.065
Acuvue Advance	Galyfilcon A	HEMA+PDMS+DMA+PVP	47	No (I)	60	No	0.070
Equis 60	Hioxifilcon A	HEMA+GMA	59	No (II)	24	No	0.13
Acuvue 2	Etafilcon A	HEMA+MA	58	Yes (IV)	28	No	0.084
SPH4UV	Hioxifilcon B	HEMA+GMA	49	No (I)	15	No	
Proclear	Omafilcon A	HEMA+PC	62	No (II)	32	No	0.065
Osmo 2		p(GMA)+HEMA+MA	72	Yes (IV)	45	No	0.14
Actifresh 400	Lidofilcon A	MMA+VP	73	No (II)	36	No	0.120
Precision UV	Vasurfilcon A	MMA+VP	74	No (II)	39	No	0.140

USAN, United States Adopted Names Council; EWC, equilibrium water content; DK, oxygen permeability; ST, surface treatment; TD, total diameter; BCR, base curve radius; CT, central thickness. Dk measurement units ($\times 10^{-11}$ (cm^2/s)[mL O$_2$/(mL $\times$ mmHg)]); DMA, *N,N*-dimethyl acrylamide; GMA, glycerol methacrylate; HEMA, 2-hydroxyethyl methacrylate; MA, methacrylic acid; MMA, methyl methacrylate; NCVE, *N*-carboxyvinyl ester; PC, phosphorylcholine; TRIS, 3-methacryloxy-2-hydroxypropyloxy propylbis(trimethylsiloxy)methylsilane; TPVC, tris-(trimethylsiloxysilyl) propylvinyl carbamate; PBVC, poly[dimethysiloxy] di [silylbutanol] bis[vinyl carbamate]; VP, *N*-vinyl pyrrolidone.

All lenses are produced with cast-molding technology except lenses made in Hioxifilcon A, B, and p(GMA)–HEMA+MA copolymer, produced by lathe-cut. Some of the principal hydrophilic monomers included in each material are also quoted along with the main monomeric chain.

holder with the approximate curvature of the contact lenses in order to simulate the lens on the ocular surface with only the anterior surface directly exposed to air. The total time the samples were exposed to air prior to measurements were initiated was less than 10 s in order to minimize dehydration before first reading could be obtained. After the lens and holder were placed on the balance, there was an additional 2–3 s until the digital scale of the balance stabilized. For repeated measures of the same lens, a minimum time interval of 72 h for the lenses to fully rehydrate.

Quantitative Descriptors and Dehydration Curves

Different quantitative parameters were derived from the curves of percentage cumulative loss of weight (CD) according to Eq. (1) (Figure 1), dehydration rate (DR) computed from Eq. (2) (Figure 2), and valid percentage dehydration (VD) computed from Eq. (3) (Figure 3). These parameters are described in detail in the following sections. To get a more reliable idea of the short-term dehydration process, the first 20 min of the dehydration process for the three dehydration curves (averaged at intervals of 5 min) will be analyzed in the last part of the results section.

Each curve presented in this work is the average of three measurements carried on three different samples of each material from the same batch.

Cumulative Dehydration as [%]

This parameter represents the accumulated loss of weight experienced by each lens at 1-min intervals during the dehydration process. It is computed using Eq. (1) where $W_{\mathrm{T}(n)}$ is the sample weight at time n with intervals of 1 min, and $W_{\mathrm{T}(0)}$ the initial sample weight. Negative values are obtained for this parameter. An example of this curve is shown in Figure 1.

$$\mathrm{CD} = \left[\frac{(W_{\mathrm{T}(n)} - W_{\mathrm{T}(0)})}{W_{\mathrm{T}(0)}}\right] \times 100 \qquad (1)$$

DR as [% Per Minute]

This parameter represents the DR per minute for each lens at a certain time during the dehydration process. It is computed using Eq. (2), where $W_{\mathrm{T}(n)}$ is the sample weight at time n with intervals of 1 min and $W_{\mathrm{T}(n-1)}$ the sample weight at time $n-1$ with intervals of 1 min. An example of this curve is shown in Figure 2. Times to achieve DR of -1, -0.5, -0.1 and -0.05% per minute are identified for each DR curve along with other quantitative descriptors.

$$\mathrm{DR} = \left[\frac{(W_{\mathrm{T}(n)} - W_{\mathrm{T}(n-1)})}{W_{\mathrm{T}(n)}}\right] \times 100 \qquad (2)$$

In Figure 2, three phases are identified for the majority of the lenses. Phase I is the part of the dehydration curve (in DR units) characterized by a high and relatively stable

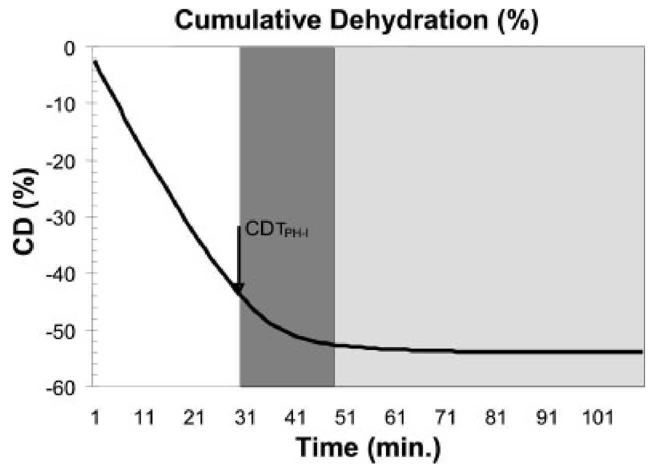

Figure 1. Curve displaying CD. Units of CD are percentages. The parameter T_{PH-I} is deduced from the profile of the DR curve showed in Figure 2.

average DR; phase II is the part of the dehydration curve (in DR units) characterized by a rapid and progressive decrease in the DR. End of phase II was arbitrary established when DR reaches −0.25% per minute; phase III is the part of the DR curve characterized by DR approaching to zero. T_{PH-I} and T_{PH-II} are duration of phase I and phase II, respectively. During phase II and phase III four additional parameters have been defined: $T_{-1\%/min}$, $T_{-0.5\%/min}$, $T_{-0.1\%/min}$, and $T_{-0.05\%/min}$ are the time to reach a DR of −1%/min, −0.5%/min, −0.1%/min, and −0.05%/min, respectively.

Valid Dehydration as [%]

This parameter represents the loss of weight of each lens at a certain time during the dehydration process compared to its total loss of weight. It is computed using Eq. (3) where $W_{T(0)}$ is the initial sample weight, $W_{T(n)}$ is the sample weight at time n with intervals of 1 min, and $W_{T(f)}$ the final lens weight. Positive values are obtained because this value

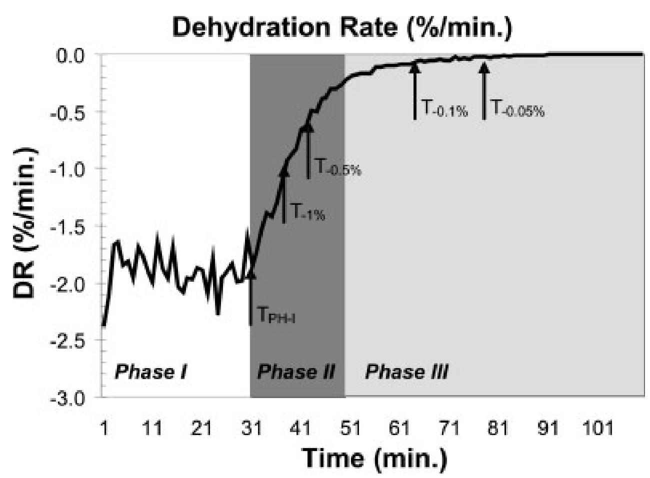

Figure 2. Curve displaying DR until stabilization. Units of DR are percentage per minute.

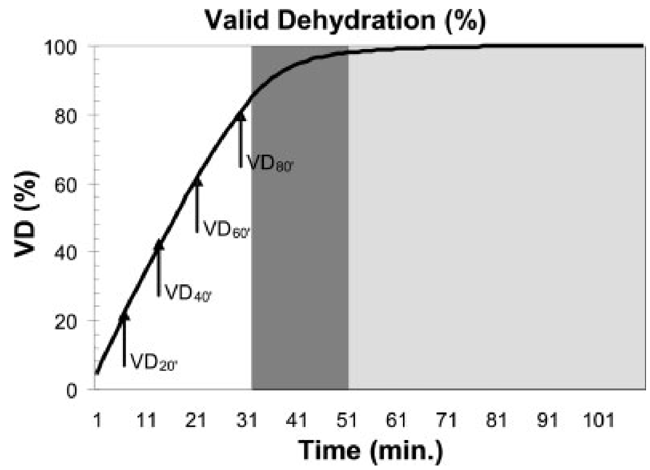

Figure 3. Curve displaying VD. Units of VD are percentages.

is calculated with respect to the final weight of the sample. An example of this curve is shown in Figure 3. Time to achieve VD of 20 ($VD_{20'}$), 40 ($VD_{40'}$), 60 ($VD_{60'}$), and 80% ($VD_{80'}$) was determined for each lens.

$$VD = \left(\frac{W_{T(0)} - W_{T(n)}}{W_{T(0)} - W_{T(f)}}\right) \times 100 \tag{3}$$

Water Retention Index

This parameter represents the difficulty of water to leave the contact lens. As a preliminary approach we have derived two values of WRI. The first one (WRI_1) was obtained from the slope of the straight line that defines the VD at 20, 40, 60, and 80 (dVD/dT) for each lens [Eq. (4)]. The second one (WRI_2) was derived from the inverse function of the mean CD during the first 5 min ($Mean_{CD}$) of the dehydration process [Eq. (5)]. This parameter will be taken as an indicator of the dehydration resistance.

$$WRI_1 = \left(\frac{dVD}{dT}\right) \times 100 \tag{4}$$

$$WRI_2 = \left(\frac{1}{Mean_{CD}}\right) \times 100 \tag{5}$$

Statistical Analysis

Values of CD, DR, and RD were compared for different contact lenses according to their EWC (low EWC, 24–38%; medium EWC, 39–60%; and high EWC, 61–74%, and type of material (conventional hydrogel, hydrogels that supposedly minimize water release, and silicone-hydrogels) using one-way ANOVA test. Before statistical tests could be applied, normal distribution of variables was assessed by Kolmogorov-Smirnov test. Regression analysis was used to plot the quantitative values obtained in this work against EWC in order to detect statistical relationships that

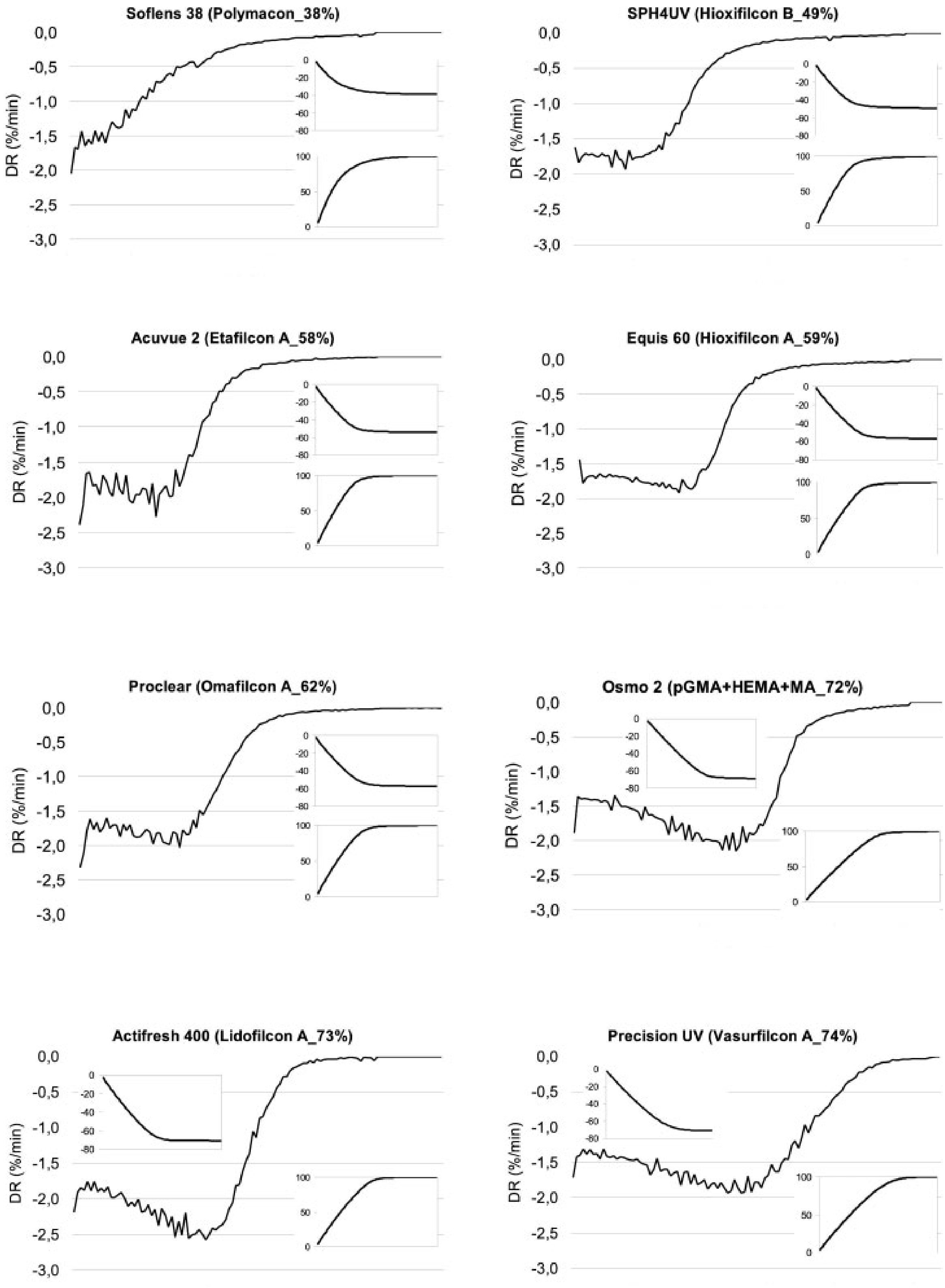

Figure 4. Curves of DR for conventional hydrogel materials. Insets represent CD (0 to −80% scale) and VD (0–100% scale).

describe the dehydration process as a function of the material EWC. Statistical significance of those correlations was assessed by Pearson correlation. Most graphical representations were made against the EWC of the contact lenses. This has a double advantage providing a quantitative reference value for statistical comparisons and at the same time

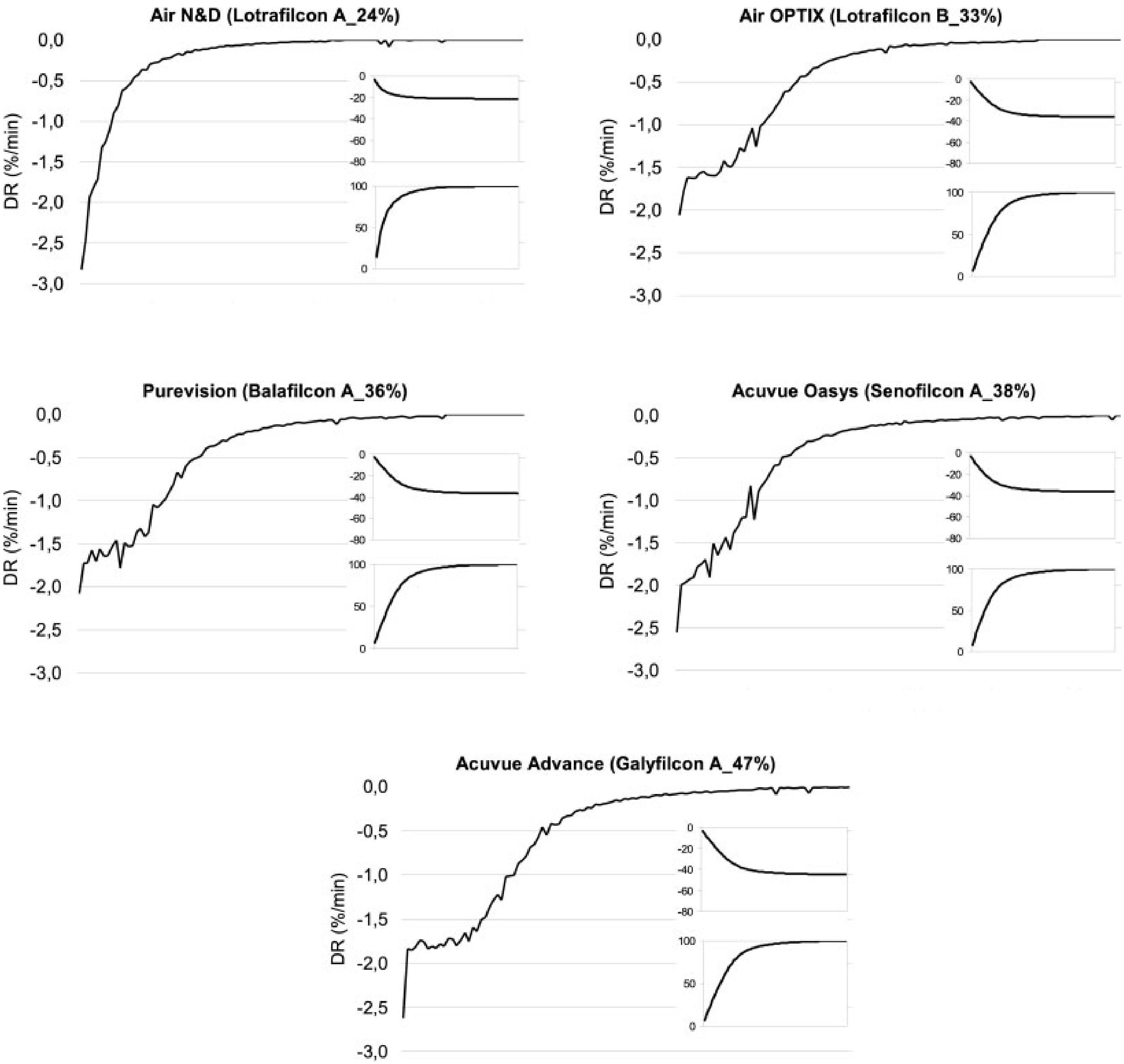

Figure 5. Curves of DR for silicone hydrogel materials. Insets represent CD (0 to −80% scale) and VD (0–100% scale).

identify each lens on graphical plots (except for two different lenses that have the same EWC = 38%).

RESULTS

Curves of DR are characteristic of each contact lens, apparently depending on their water content and polymeric composition. In those curves a three-phase pattern is observed. Phase I is characterized by a relatively uniform DR, and has a limited duration. An exception to this behavior is lotrafilcon A lens, with no defined phase I. Phase II is characterized by a rapid and almost linear decrease in the DR. Phase III represents the final period of time in which the lens approaches a zero DR. There is not a distinct change between phase II and III, so this point was set arbitrarily as the point where DR achieves a value of −0.25%.

Figures 4 and 5 present the DR curves for conventional hydrogels and silicone-hydrogel materials, respectively. From the DR curves, we determine the duration of phase I as the point where DR begins to decrease. High water content materials presented a significantly longer phase I (44.5 ± 10.97 min) compared to medium EWC (22.75 ± 7.32 min) and low EWC (12 ± 3.91 min). These differences were statistically significant between low and high water content materials (ANOVA; $p = 0.001$).

Duration of phase I is plotted in Figure 6(a) against the EWC of the lenses displaying a strong relationship (r^2 =

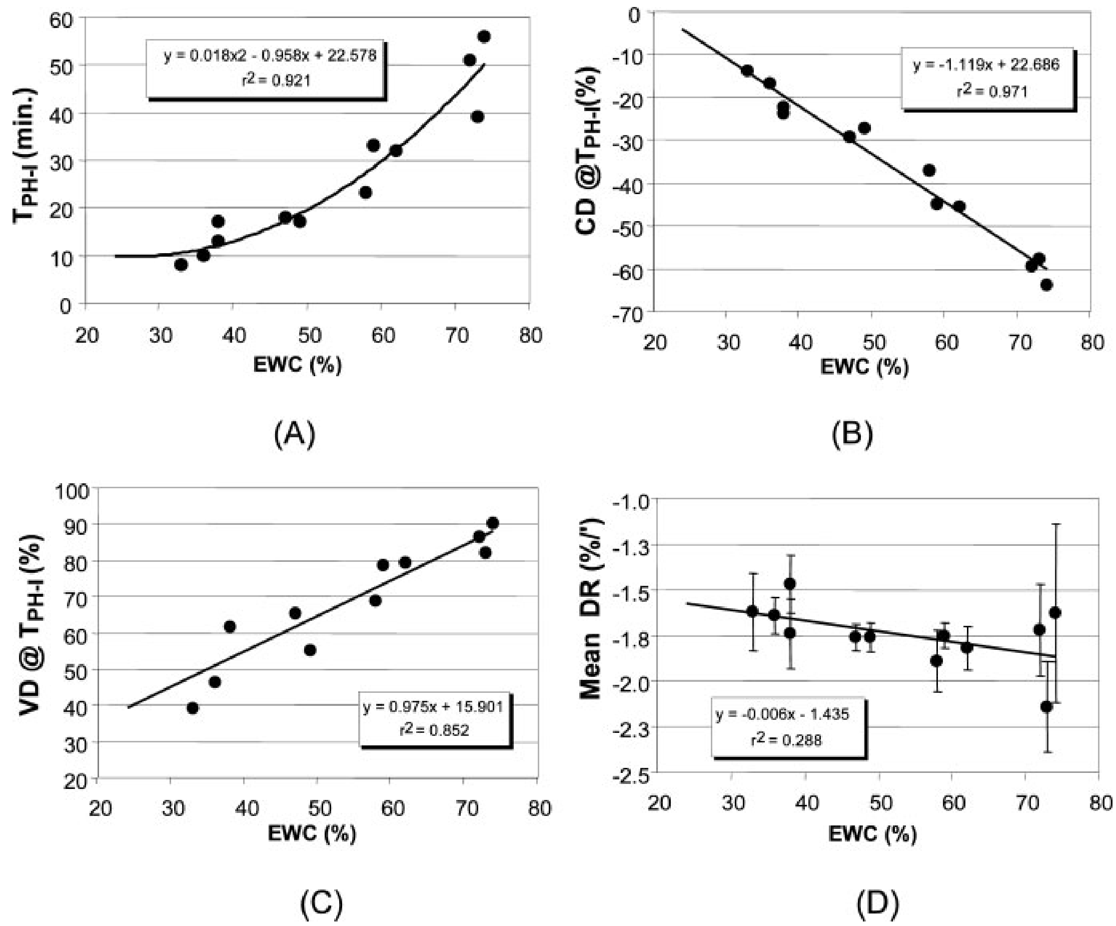

Figure 6. Relationship of EWC of contact lens materials with duration of phase I (A), CD (B) and VD at the end of phase I (C), and mean DR during phase I (D). Bars represent standard deviation.

0.921). A second order polynomial function fits to this relationship (T_{PH-I} vs. EWC) showing a rapid increase in duration of this phase as EWC of the lenses increase. The minimum value of the function seems to be around an EWC of about 20%. CD and VD at the end of phase I are strongly correlated with EWC as seen in Figure 6(b,c). Mean DR during phase I is plotted against EWC in Figure 6(d); in this case despite a trend towards higher DR during phase I for lenses with higher EWC, the correlation was not significant (Pearson coefficient $= -0.536$; $p < 0.072$). These parameters and their relationship with EWC over the

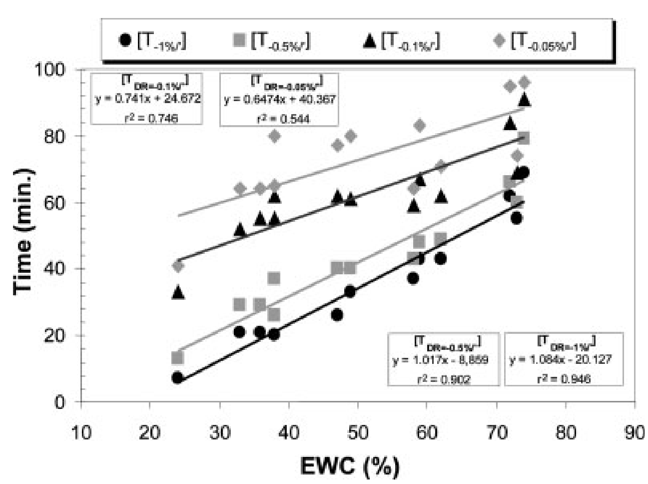

Figure 7. Time to achieve a DR of −1, −0.5, −0.1, and −0.05%/min against EWC.

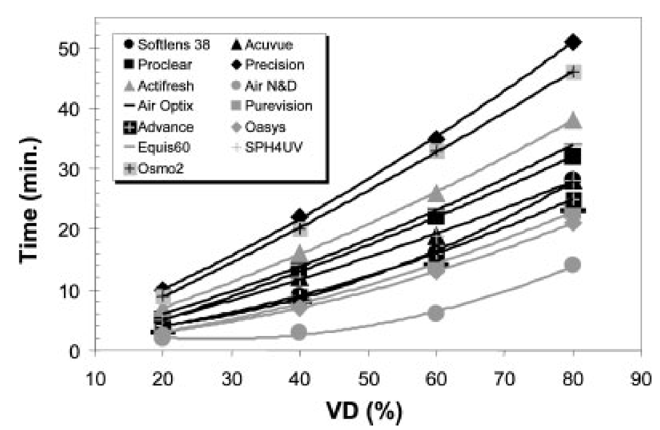

Figure 8. Time to achieve VD of 20, 40, 60, and 80% for different contact lens materials.

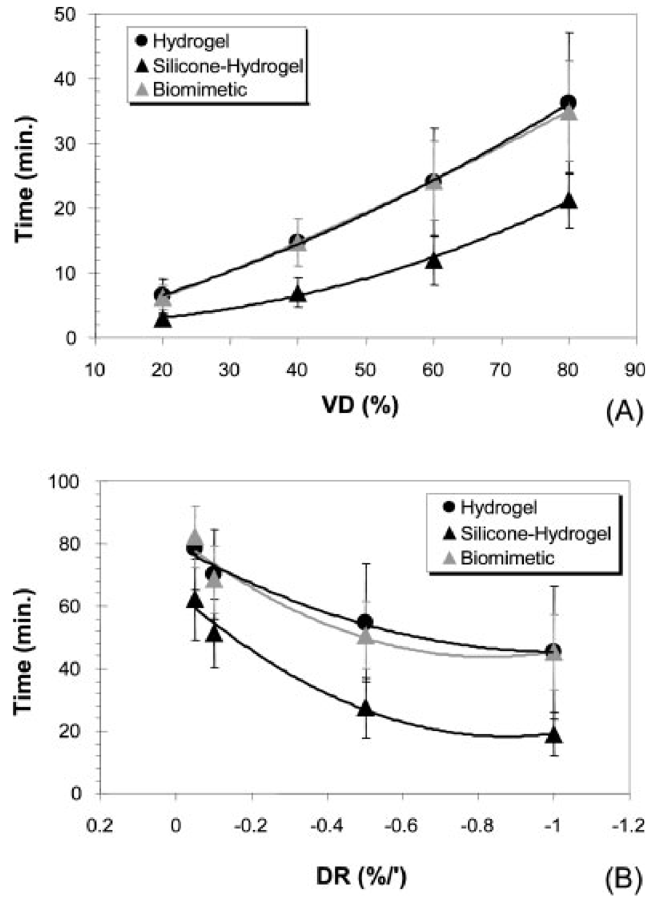

Figure 9. Mean and standard deviation values of time at VD of 20, 40, 60, and 80% (A) and time for DR of −1, −0.5, −0.1, and −0.05%/min (B) for silicone-hydrogel lenses, lenses claimed to reduce on-eye dehydration (biomimetic), and conventional hydrogels. Bars represent standard deviation.

first 20 min of the dehydration process will be further analyzed later in this section.

Times to achieve a DR of −1, −0.5, −0.1, and −0.05% per minute during phases II and III, were plotted against EWC and fitted to linear models as independent variable in Figure 7. According to this figure, the time to reach each DR landmark follows a more predictable linear relationship for the first two parameters ($T_{-1\%/\mathrm{min}}$ and $T_{-0.5\%/\mathrm{min}}$) than the other two ($T_{-0.1\%/\mathrm{min}}$ and $T_{-0.05\%/\mathrm{min}}$).

We also evaluated the time required to achieve a VD of 20, 40, 60, and 80 for each material tested. Time values follow almost ideal correlations ($r^2 \geq 0.99$) when fitted to a 2nd order regression equation for all the materials under investigation. Figure 8 shows that differences are evident among different materials. It is also evident that differences become larger for higher values of dehydration. Two lines are hidden by others as SPH4UV exactly matches values of Acuvue 2 and Air Optix exactly matches values of Purevision. Coefficients of determination are 0.999 or 1.0 for all materials except lotrafilcon A ($r^2 = 0.995$). Values of time to reach VD of 20, 40, 60, and 80% were highly correlated with EWC ($r = 0.921$, $r = 0.944$, $r = 0.940$, $r = 0.914$) and statistically significant ($p < 0.001$ in all cases). As expected, the most significant difference was observed between the least hydrated silicone-hydrogel lens (lotrafilcon A, 24% EWC), and the most highly hydrated hydrogel lens (vasurfilcon, 74% EWC). While the least hydrated silicone-hydrogel (lotrafilcon A) reached each VD landmark the fastest, vasurfilcon (74% EWC), and GMA/HEMA/MA (72% EWC) showed a significantly slower progression towards the higher VD values than the remaining materials, including one with similar EWC, lidofilcon A (73% EWC).

These differences are further explored by grouping the lenses by their EWC and polymeric composition as shown in Figures 9 and 10. On average, the parameters described in the previous paragraph have lower average values for the silicone-hydrogel materials than for HEMA-based hydrogels. Figure 9 shows this trend, with silicone-hydrogel materials displaying shorter time periods to achieve each valid dehydration (VD) value and lower DRs, respectively. Conversely, the mean behavior of all the conventional hydrogels, including those claimed to retard dehydration, is almost indistinguishable regarding these parameters.

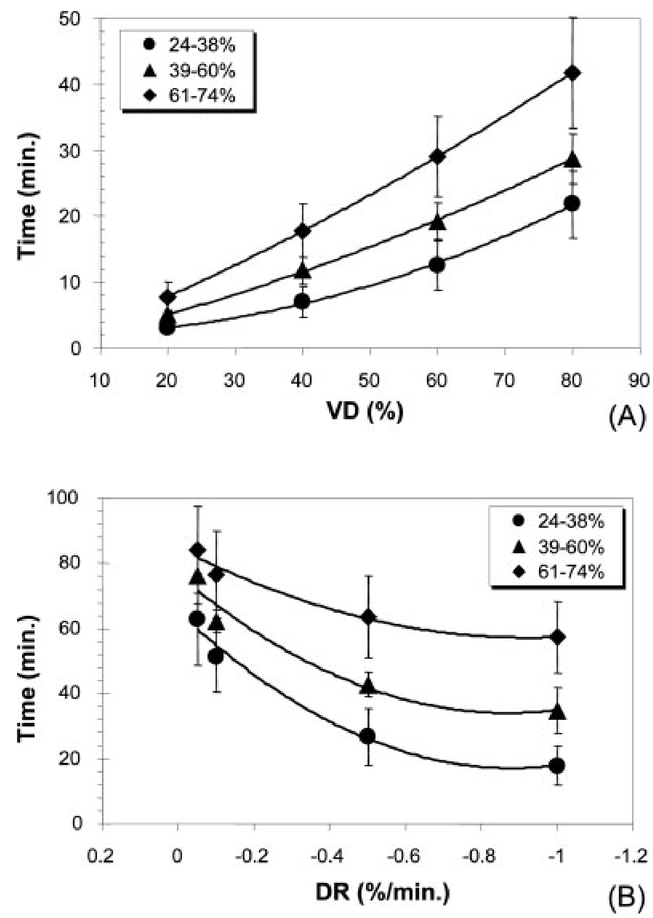

Figure 10. Mean and standard deviation values of time at VD of 20, 40, 60, and 80% (A) and time for DR of −1, −0.5, −0.1, and −0.05%/min (B) for lenses within the three groups according to their EWC. Bars represent standard deviation.

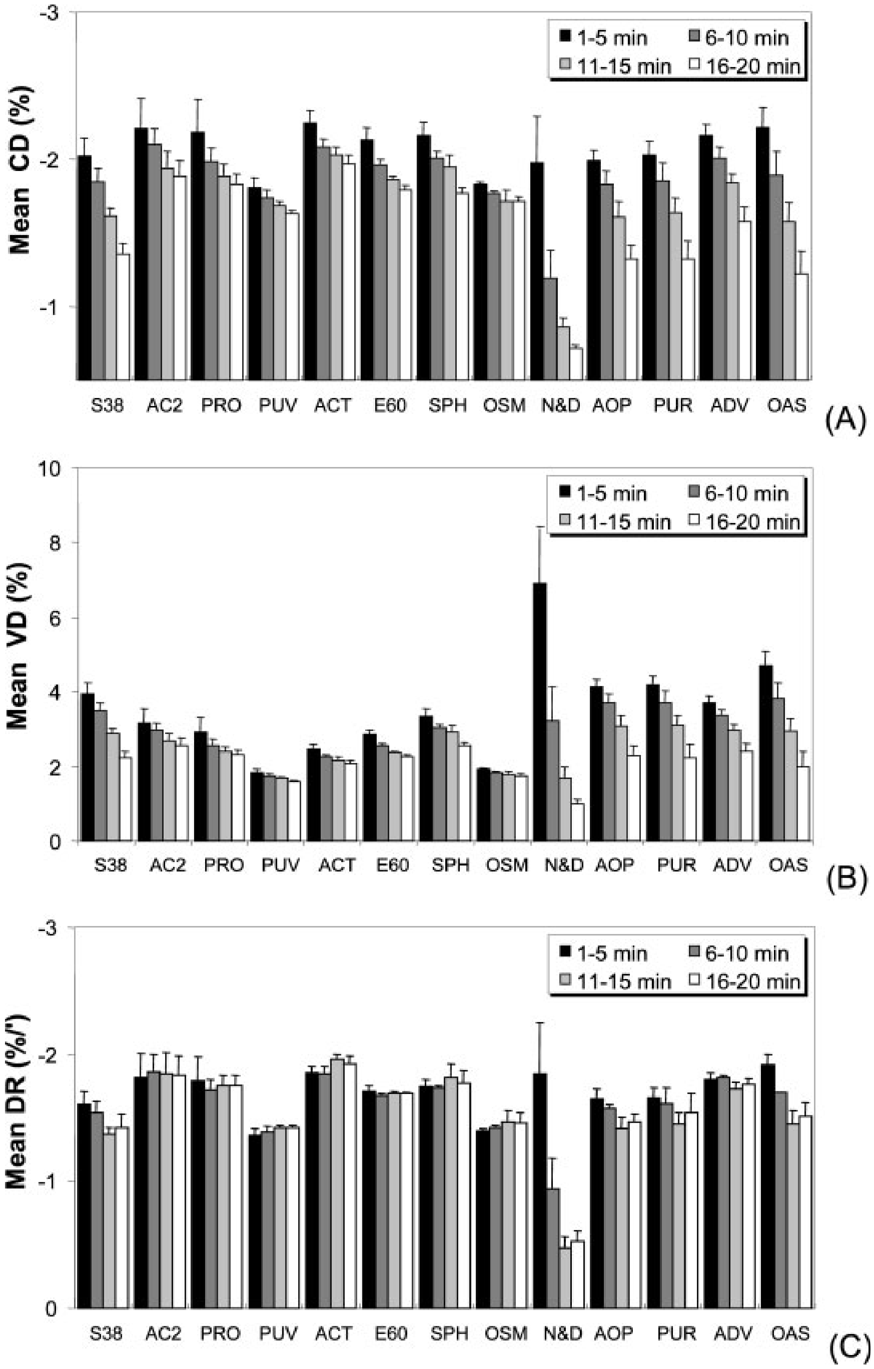

Figure 11. Mean and standard deviation of CD (A), VD (B), and DR (C) at intervals of 5 min for the first 20 min. Bars represent standard deviation. Legend: HEMA-based lenses: S38 (Soflens, 38–38%); AC2 (Acuvue 2–58%); PRO (Proclear, 62%); PUV (Precision UV, 74%); ACT (Actifresh, 400–73%); E60 (Equis, 60–59%); SPH (SPH4UV, 49%); OSM (Osmo 2–72%). Silicone-hydrogel: N&D (Air Night & Day, 24%); AOP (Air Optix, 33%); PUR (Purevision, 36%); ADV (Acuvue Advance, 47%); OAS (Acuvue Oasys, 38%).

In Figure 10 the mean values for the same parameters are now represented for lenses grouped by their EWC in low EWC (24–38%), medium EWC (39–60%), and high EWC (61–74%). As expected from the previous analyses, all differences were statistically significant (ANOVA, $p < 0.05$) except for time to achieve DR of -0.1%/min ($p = 0.072$) and -0.05%/min ($p = 0.074$).

To get more precise knowledge of the short-term dehydration process for each particular lens, we divided the first 20 min of the dehydration process into 5 min periods, and CD, VD, and DR were averaged within those periods. Mean values and standard deviation are presented in Figure 11(a–c), and plotted against the EWC in Figures 12, 13, 14, respectively. Average CD and VD decreased for all

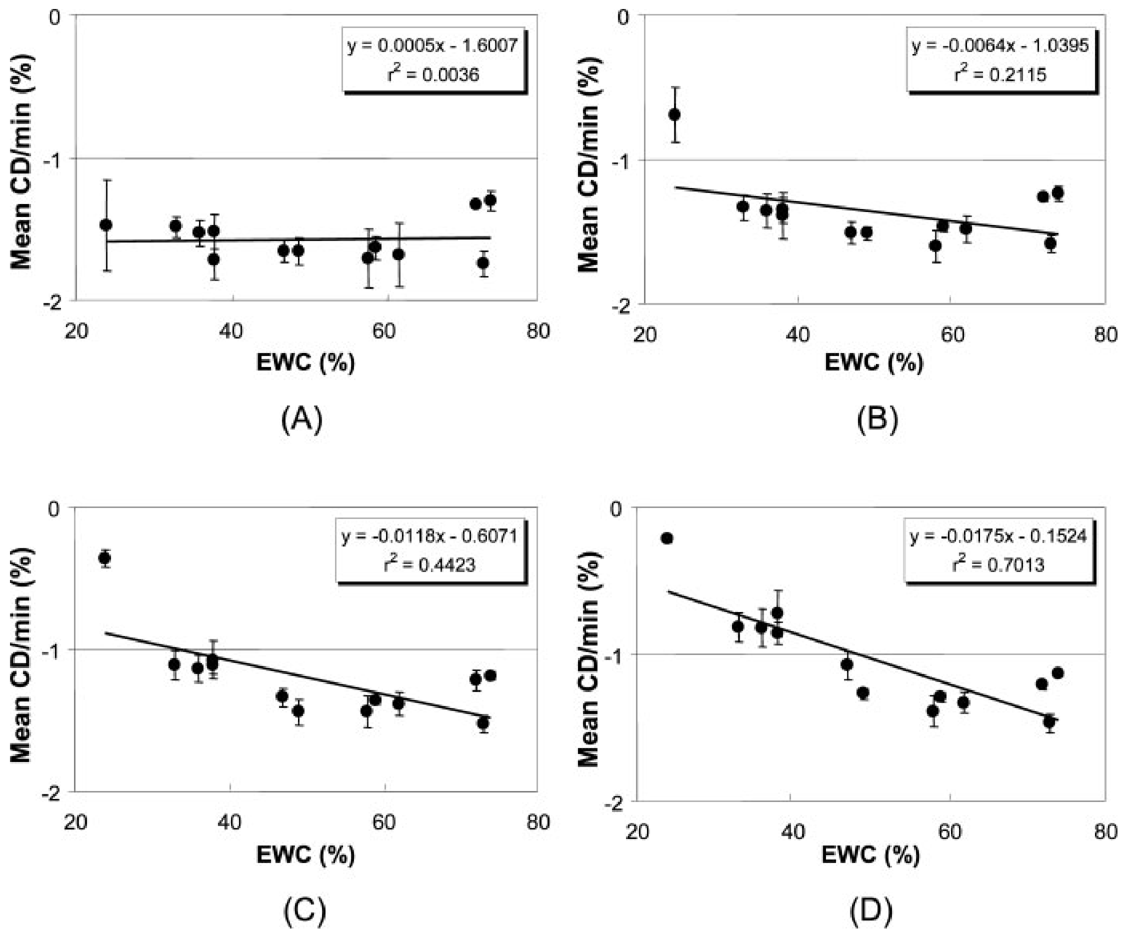

Figure 12. Relationships between EWC of the contact lenses and mean CD at intervals of 5 min for the first 20 min of the dehydration process during 1–5 (A), 6–10 min (B), 11–15 (C), and 16–20 min (D). Bars represent standard deviation.

lenses between the first period (1–5 min) and the forth period (16–20 min). This decrease was the most obvious for silicone hydrogel materials, and less marked for high water content PUV and OSM lenses [Figure 11(a,b)]. The mean DR is fairly uniform for HEMA-based hydrogels. However, decrease is seen for some silicone-hydrogel materials [Figure 11(c)].

For average CD (see Figure 12), significant correlations with EWC were found only for the 3rd (11–15 min, Spearman coefficient = 0.682, $p = 0.010$) and 4th period (16–20 min, Pearson coefficient = 0.837, $p < 0.001$). Conversely, for VD, significant correlations with EWC were found during the 1st (1–5 min, Pearson coefficient. = 0.914, $p < 0.001$) and 2nd period (6–10 min, Pearson coefficient = 0.901, $p < 0.001$) as shown in Figure 13. Figure 14 shows that DR is quite similar during the first 5 min, and thereafter shows a trend for higher dehydration at higher EWC.

Figure 15(a,b) show two different approaches to the determination of the water retention index (WRI) or index of dehydration resistance. The first one is clearly correlated with contact lens EWC ($r = 0.897$; $p < 0.001$) while the second one is not ($r = 0.128$; $p = 0.676$). Values of both WRI indices were also evaluated for potential correlations with central lens thickness. Again, WRI by the first model showed a correlation with lens thickness ($r = 0.653$; $p < 0.015$) while the second one is not correlated with lens thickness ($r = 0.419$; $p = 0.154$).

DISCUSSION

The ability of a contact lens to maintain its hydration during wear is considered as one of the most important parameters involved in contact lens tolerance. Currently, different materials are available, with low, medium and high water content. Most HEMA-based conventional hydrogels have an EWC ranging from 38 to 74%. This group includes lenses which claim to retain normal hydration better than other types of hydrogel lenses. Silicone-based hydrogel lenses, which differ in proportion and types of siloxane moieties and hydrophilic components, have an EWC ranging from 24 to 47%.

Within a polymer, water molecules can be “bound” to one another and to hydrophilic groups on the polymer backbone by hydrogen bonds, or can be “free,” only loosely associated with each other and without any poly-

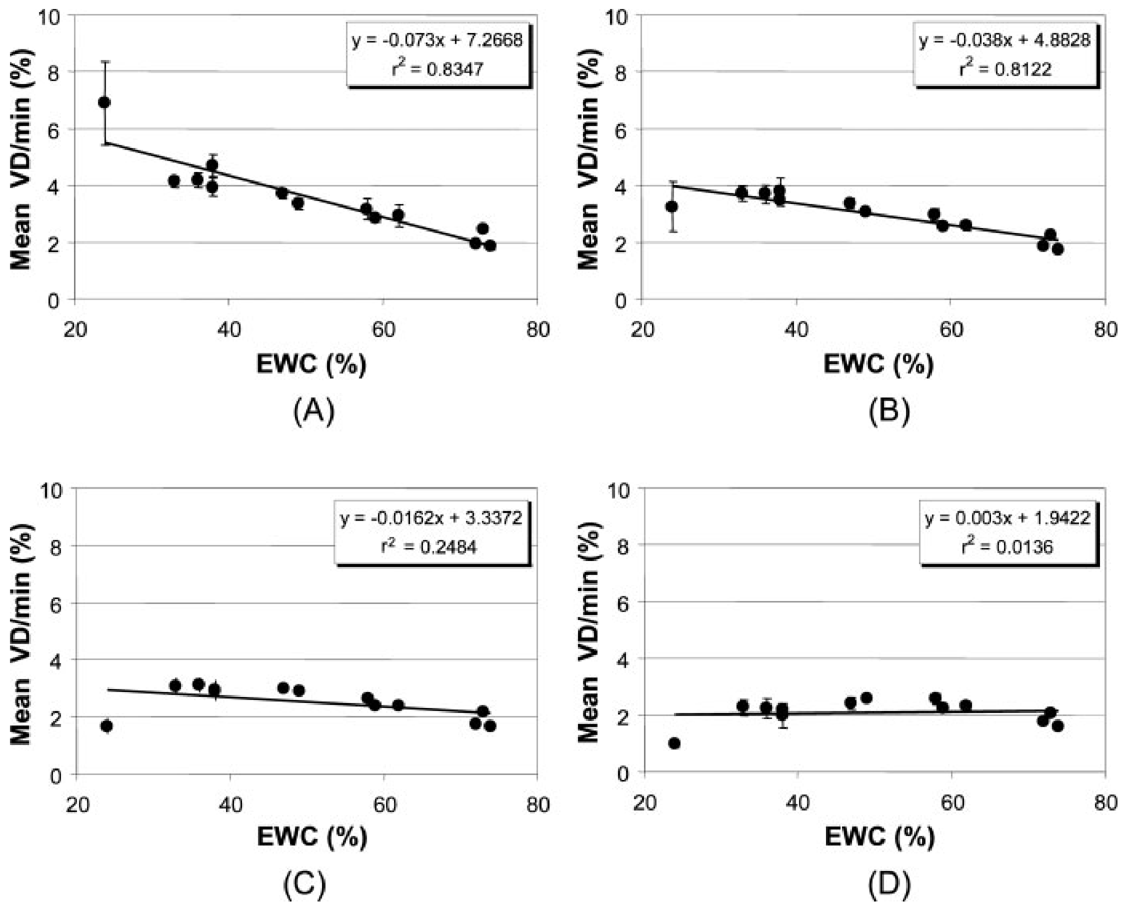

Figure 13. Relationships between EWC of the contact lenses and mean VD at intervals of 5 min for the first 20 min of the dehydration process during 1–5 (A), 6–10 min (B), 11–15 (C), and 16–20 min (D). Bars represent standard deviation.

meric structural effects. However, the reported amount and proportion of "bound" and "free" water depends largely on the method used for determination. According to Refojo, in one high water content hydrogel (EWC 70%) more than half was "free" water, while within low to medium EWC hydrogels (EWC 41–45%) the proportion of "free" to "bound" water was inverted.[28] Despite all the water in a hydrogel can be removed by evaporation under the right conditions, in clinical terms, only the "free" water is physiologically relevant to contact lenses. Current research has showed that the proportion of not-bound or freezable water is positively correlated to the EWC of the material.[29,30]

This is the first study presenting qualitative and quantitative descriptors for the *in vitro* dehydration process of such a wide range of currently available contact lenses in their original design. In our opinion, graphs presenting DRs are the best way to characterize the dehydration process of hydrogel contact lenses. Those graphs show a three-phase profile with an initial phase I of rapid and relatively constant DR, a phase II of rapid and progressive decrease of DR and a final phase III characterized by a slow decrease of DR approaching to zero. However, during phase I, DR experiences constant variations within a maximum and minimum range around the average DR reported here. A similar feature is observed in the % dehydration curves reported by Jones et al.[26] In our opinion this acceleration and slow-down in DR would be related to the water loosely bound to the surface of the polymer.

Only one silicone-hydrogel lens, lotrafilcon A, displayed a different dehydration behavior compared to all the other hydrogel lenses examined in this study. There was no phase I observed in its DR curve. This phenomenon could be explained on the basis of its higher content of siloxane moieties compared to the other silicone-hydrogel lenses tested and its lower EWC. The cause of the water retention in this lens could also be due to the hydrocarbon-plasma coating that, by reacting with air, results in a thin hydrophilic membrane over the surface of the lens.[31] As this thin layer of water dehydrates the inner dehydration of the polymer will begin thus passing directly to phase II with no apparent phase I. Other potential explanation to this fact is that silicone rubber has been shown to have high water pervaporation, but this does not appear to contribute to liquid water transport though silicone hydrogel lenses.[9] Also, while the so-called silicone-hydrogels contain polysiloxane (silicone) and, or other siloxane moieties, they do not contain silicone rubber per se.

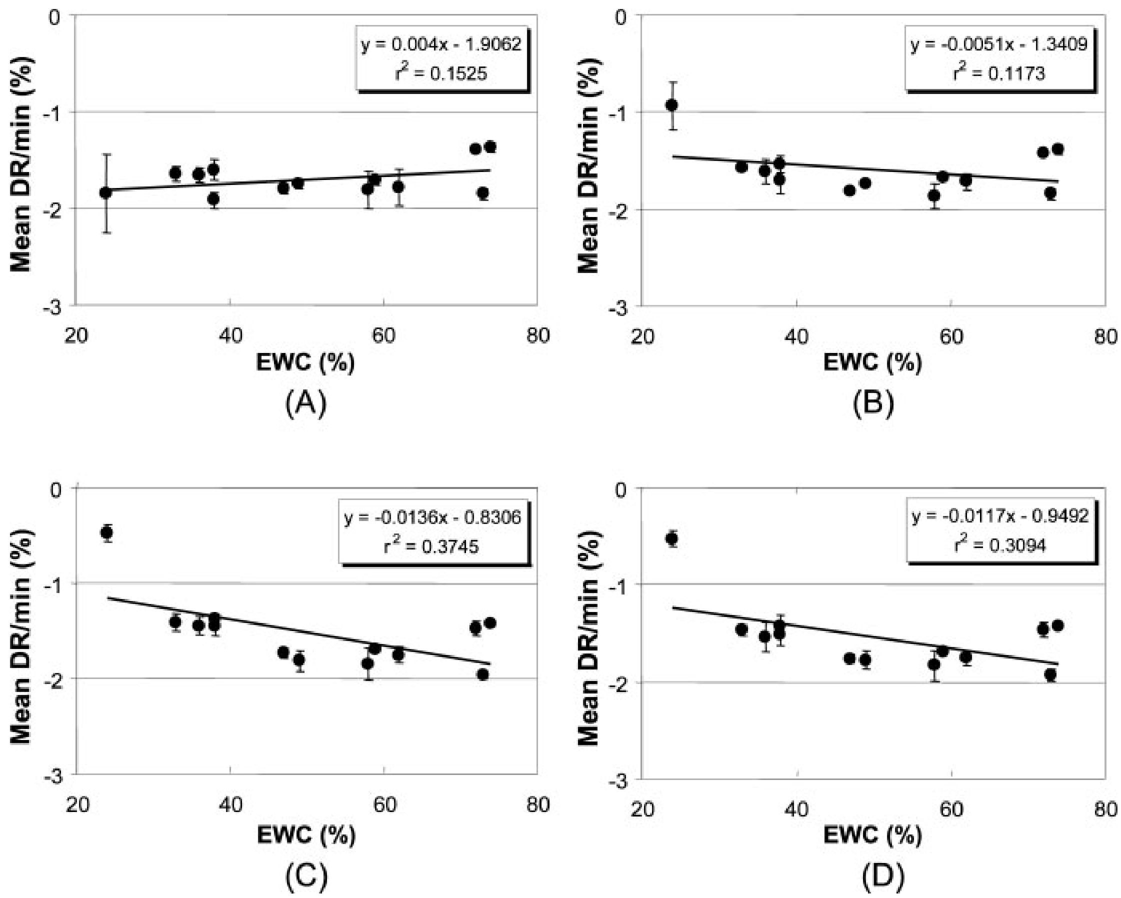

Figure 14. Relationships between EWC of the contact lenses and mean DR at intervals of 5 min for the first 20 min of the dehydration process during 1–5 (A), 6–10 min (B), 11–15 (C), and 16–20 min (D). Bars represent standard deviation.

The other silicone-hydrogel materials have a brief but defined phase I, which lengthens as the water content increases (siloxane content decreases). Thus, the presence of phase I is a characteristic of all conventional hydrogels, but not of silicone-hydrogels containing high proportions of siloxane moieties.

The results and relationships presented in this work support many of the observations of previous clinical and experimental studies. According to our results, the higher the EWC of hydrogels the higher the DR and the longer the duration of phase I. This means that the higher the EWC of the hydrogel lenses, the higher cumulative and VD within the same time periods when compared to lower water content hydrogels.

The higher dehydration of more hydrated hydrogels, despite not admitted by all authors, is the most commonly accepted relationship between EWC of hydrogels and DR.[10] Andrasko concluded that at same lens thickness, hydrogel lenses with higher water content dehydrate more during the same time period of *in vivo* lens wear than lenses of lower EWC.[8] McConville and Pope studied the diffusivity of water in hydrogels and concluded that this property was well predicted by their EWC.[32] The authors suggested that the mobility of water within the hydrogel is associated with the probability of the water to leave the bulk of the hydrogel, thus supporting the commonly accepted fact that high water content contact lenses dehydrate more in the eye than the lower hydrated lenses. Jones et al.[26] used a methodology similar to ours to evaluate the dehydration of three conventional hydrogels and two silicone-hydrogel contact lenses. However, they used different environmental conditions of RH and airflow. They observed that *in vitro* dehydration of hydrogels was closely related to the EWC, and as a consequence, silicone-hydrogels dehydrated less than high water content hydrogels. The results derived from our *in vitro* dehydration curves support these observations.

In a study with etafilcon A (HEMA/VP, and 58% EWC) and omafilcon A (HEMA/phosphorylcholine (PC) moieties, and 62% EWC) under arid and arctic environments, significantly higher in-eye dehydration was found for the etafilcon A lens.[33] Another study found similar results under normal wearing conditions.[34] Our results predict a difference of DRs of about 0.07% per minute between these two lenses, supporting the higher dehydration of etafilcon A despite its slightly lower EWC compared to omafilcon A, probably due to the PC moieties in the former material. However, considering the present results alone, we cannot predict that

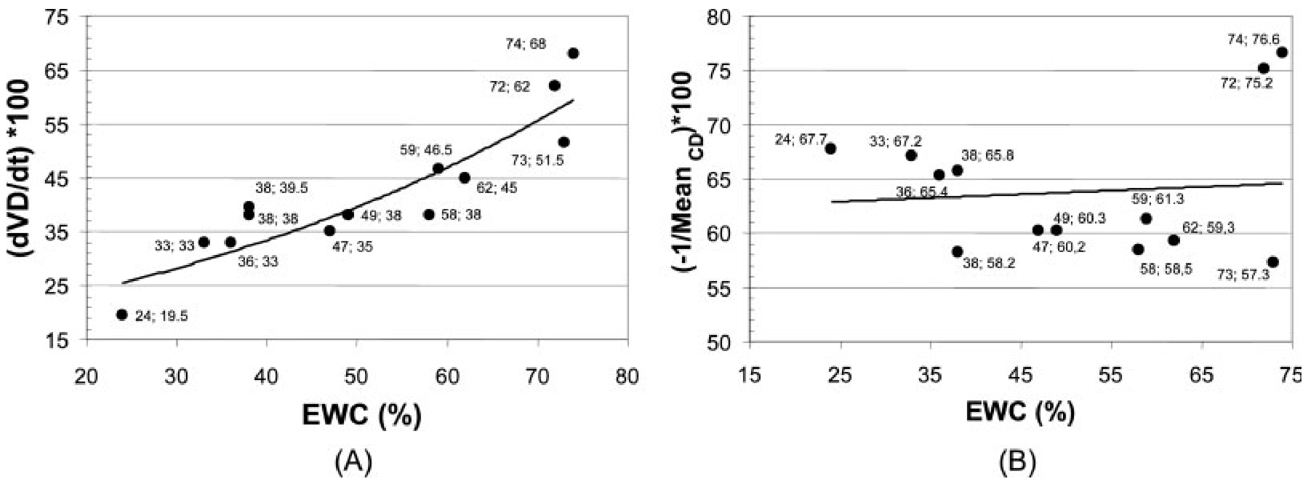

Figure 15. WRI as a function of EWC. First calculation was computed from the slope of straight lines fitted to the VD at 20, 40, 60, and 80 min for each lens (A). Second calculation was computed as inverse function of the mean CD during the first 5 min (B).

such a small difference will have significant implications from the clinical point of view.

Another experimental study carried out by Maldonado-Codina and Efron concluded that hydrogel contact lenses with lower water content had lower free-to-bound water ratio than the more hydrated lenses.[30] The same conclusions were previously reported by Tranoudis and Efron.[29] Although, the present study did not specifically measured the free and bound portions of water in the hydrogel lenses, it is reasonable to conclude that free water would be lost first, during the rapid phase I within the dehydration process. This is supported by the higher dehydration (both CD and VD) and longer duration of phase I obtained for hydrogels with higher EWC. Our dehydration curves display a different behavior between phase I, at a sustained higher rate of dehydration, and phase II, with a rapid decay in DRs approaching zero at end of phase III. The first two phases could be in some way related to the evaporation of freezable and nonfreezable water.

A clinical study from Morgan and Efron, compared the dehydration of etafilcon A (conventional hydrogel, 58% EWC) and balafilcon A (silicone-hydrogel, 36% EWC). After a period of 2 weeks of lens wear, water content of etafilcon A decreased by 10.3% while the balafilcon lens decreased by only 8% of their initial water content. Considering the higher EWC of the etafilcon A compared to the balafilcon A, the result of the *in vivo* study could be expected. Nevertheless, if we consider the VD values, greater differences are found, between the results of etafilcon A and balafilcon A with VD values of 6.0 and 2.8% of their respective EWC.[5] In this regard, our results predict an almost double average cumulative dehydration (CD) of etafilcon compared to balafilcon, thus are in total agreement with those results.

In the work of Tranoudis and Efron, the authors evaluated lens centration, up-gaze lag, post-blink movement, total diameter and subjective assessment of comfort for eight hydrogel lenses made of different materials. They found that all lenses exhibited a reduction in lens total diameter and most of the lenses exhibited less movement on blinking and less lag after a 6-h wearing period. All these facts can be directly related to on-eye contact lens dehydration.[35]

In the present study, we have obtained significantly different results of dehydration of lenses at the mid-term (end of phase I and phase II, 30–50 min) and long-term (phase III, 100 min), but we have observed a quite similar average CD during the first 5 min for all lenses, irrespective of their composition and EWC. The initial dehydration observed under *in vitro* conditions could be the most representative of the *in vivo* dehydration of the contact lenses. Thus, despite a sharp trend towards higher dehydration as the materials increase their EWC, such differences would not be as sharp at the first stages of the process. This fact, and the different experimental conditions used by different authors, could explain some of the controversies surrounding the ability to confirm statistically significant differences in dehydration among different contact lens materials.[36]

In conclusion, most of the dehydration parameters obtained here support a lower DR of silicone-hydrogel materials, which is in agreement with other recent studies.[5] However, there is no significant difference in dehydration when we compare silicone-hydrogel lenses and conventional hydrogels of similar EWC (i.e. senofilcon A, balafilcon A and polymacon), suggesting that the EWC more than the polymeric composition governs the ability of contact lenses to sustain their hydration.

Regarding the comparison between conventional hydrophilic lenses and lenses which claim to retain water better than the other HEMA based lenses, we only observed difference between omafilcon A, containing PC, and etafilcon A, both of which have a similar water content. We observed that omafilcon A displayed a lower average DR during phase I and slightly longer time periods to achieve certain degrees of VD than etafilcon A. This observation is in agreement with clinical and experimental results presented by Young et al.[13]

The parameter we have designated as WRI can be used as a quantitative indicator of the lens resistance to dehydration. The second equation used in the present work to obtain WRI (WRI_2) seems to be more useful in terms of lens physiological performance because it expresses the average dehydration (in absolute values) within the first five minutes of the dehydration process. The water evaporated during this phase is more likely to be related with the evaporation process while the lens is on the eye. Additionally, values of WRI_2 obtained have demonstrated not to depend on EWC or lens thickness. For this parameter, we can have significant differences in evaporation rates even for lenses with similar EWC. Thus, contrary to most of the previous quantitative parameters, this could reflect some differences in polymeric composition irrespective of lens EWC and thickness profile. For example, lidofilcon A (73% EWC) has shown a WRI significantly lower than lenses of similar thickness and EWC. Also, senofilcon A showed a lower WRI than polymacon, despite their similar EWC. Omafilcon A and hioxifilcon A showed WRI values slightly above etafilcon A, but those differences were too small to be statistically or clinically significant. This parameter should be further investigated and the model should be probably refined in order to better reflect the ability of the contact lens to retain its hydration in the short-term (i.e. short periods of time between blinks, ...). WRI could be improved by considering parameters as time to DR of -1, -0.5, -0.1, and -0.05% as well as duration, average DR and VD at end of phase I.

Despite some limitations, the results presented have demonstrated to be in agreement with other clinical and experimental observations made in several previously published studies regarding comfort and on-eye dehydration of hydrogels. Considering these facts, the methodology discussed in the present study has demonstrated to be sensitive and able to show significant differences in water behavior between lenses of similar EWC, but with different chemical composition.

The present study provides several objective quantitative parameters to characterize the *in vitro* dehydration process of different currently used contact lens materials. Some of these parameters help us to understand certain behaviors observed in clinic and other experimental investigations. They have also showed objective differences in the behavior of conventional hydrogels compared to hydrogels which claim to retain hydration more efficiently, and to silicone hydrogel materials of similar EWC and thickness. In addition, this approach will be useful in carrying out further experiments simulating different environmental conditions, without exposing human subjects to adverse conditions of temperature or RH.

However, the actual significance of each parameter obtained will have to be evaluated in more applied experiments in order to evaluate which ones are more adequate to characterize contact lens degradation with use or the ability of contact lens solutions to improve lenses hydration and prevent dehydration, just to cite some potential applications.

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